At Least One-Third of Poor Countries' Disease Burden is Due to Malnutrition

DISEASE CONTROL PRIORITIES PROJECT

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DISEASE CONTROL PRIORITIES PROJECT

BACKGROUND

In the late 1980s, the World Bank initiated work to inform priorities for control of specific diseases and to generate comparative cost-effectiveness estimates for interventions addressing the full range of conditions important in developing countries. The purpose of the comparative cost-effectiveness work was to provide one input into decision-making within the health sectors of highly resource-constrained countries. This process resulted in the 1993 publication of *Disease Control Priorities in Developing Countries**. A decade after publication of the first edition, the World Bank, the World Health Organization, and the Fogarty International Center (FIC) of the U.S. National Institutes of Health (NIH) have initiated a "Disease Control Priorities Project" (DCPP) that will, among other outcomes, result in a second edition of *Disease Control Priorities in Developing Countries (DCP2)*. The DCPP is financed in part by a grant from the Bill & Melinda Gates Foundation. *DCP2* is intended both to update *DCP1* and to go beyond it in a number of important ways, e.g. in documentation of success stories, in discussion of institutional and implementation issues, and in explicit discussion of research and development priorities. Publication of *DCP2* is intended for mid-2005.

*This volume was edited by Dean T. Jamison, W. Henry Mosley, Anthony R. Measham and Jose Luis Bobadilla and published by Oxford University Press in 1993.

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THE WORKING PAPERS SERIES

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DISCLAIMER

The Disease Control Priorities Project (DCPP) is a joint project of the World Bank, the World Health Organization, and the Fogarty International Center of the National Institutes of Health (U.S. Department of Health and Human Services). It is funded in part by a grant from the Bill & Melinda Gates Foundation. Conclusions conveyed in the Working Papers do not necessarily reflect those of any of the institutions listed.

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Working Paper No. 1

At Least One-Third of Poor Countries' Disease Burden is Due to Malnutrition

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Foreward

The Disease Control Priorities Project (DCPP) is pleased to initiate its Working Paper series with this paper by John B. Mason, Philip Musgrove, and Jean-Pierre Habicht entitled “At Least One-Third of Poor Countries’ Disease Burden is Due to Malnutrition”. A major purpose of the working paper series is to make available background work for the planned second edition of Disease Control Priorities in Developing Countries, to be published by Oxford University Press in 2005. Our hope in bringing background work out soon after it becomes available is that this will allow both early use by and critical reactions from a broad community of users. The authors welcome comments both directly to them or in the discussion space we have established on the DCPP Web site (www.fic.nih.gov/dcpp).

Mason et al. point out early in their paper that both dietary inadequacy and infectious disease lead to malnutrition, i.e., to inadequate physical growth or low levels in body organs of essential nutrients such as iron, iodine, or vitamin A. This observation leads directly to questions of the type that characterize the work of the DCPP: How can malnutrition be most cost effectively reduced? For a given commitment of resources would food transfers, say, lead to more of a reduction in malnutrition than would an immunization program? Mason et al. provide evidence to show how central malnutrition is for human health and why, therefore, getting the most value for money in reducing malnutrition is so important.

Those of us working on the DCPP hope you find this, and subsequent entries in our Working Paper series to be of value and that you will participate in Web-based dialogue concerning their content.

Dean T. Jamison
Senior Editor
Disease Control Priorities in
Developing Countries, second edition

AT LEAST ONE-THIRD OF POOR COUNTRIES' DISEASE BURDEN IS DUE TO MALNUTRITION[a,b]

John B Mason, Philip Musgrove, and Jean-Pierre Habicht

Abstract

The portion of the global burden of disease (mortality and morbidity, 1990 figures) in developing countries that would be removed by eliminating malnutrition is estimated as 32%. This includes the effects of malnutrition on the most vulnerable groups' burden of mortality and morbidity from infectious diseases only. This is therefore a conservative figure, but nonetheless much higher than previous estimates, mainly due to now including micronutrient malnutrition. The larger part (20%) is from malnutrition acting as a risk factor, in synergy with infectious diseases, modifying their effect on health and survival. About 10% of the burden is the direct effect of deficiencies with very high prevalences, primarily of iron (e.g. anemia affects 40 - 55% of women B non-pregnant and pregnant) and iodine (over 600 million people with goiter) causing disability. In children of 0-4 years, reducing underweight (an index of general malnutrition) would lower their disease burden by 35%, mostly by reducing mortality. Vitamin A deficiency also primarily acts as a risk factor in infant and child mortality, and eliminating it would save 16% of the burden in children. The mortality risk associated with iodine deficiency is the least well known; a few results indicate a possible 8% benefit in child mortality reduction. Eliminating severe anemia in pregnancy is estimated to reduce maternal disease burden by some 13%. The countries with the worst health and nutrition conditions -- Asia and Sub-Saharan Africa -- would gain most from the broad public health benefits of better nutrition. Seen in relation to the overall burden (all population groups, all causes, all developing countries) eliminating child underweight would save 15%, and eliminating micronutrient malnutrition (in children plus anemia in reproductive age women) an additional 18%.

Introduction

Inadequate dietary intake and infectious diseases interact to make a major contribution to the burden of disease, especially that of common infectious

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b *Acknowledgements*: We thank Curtis Florence and David Hotchkiss for help with statistical theory. At different times this work benefited from support from the World Bank, the Micronutrient Initiative, and the United Nations ACC Sub-Committee on Nutrition. We acknowledge the encouragement of the late Dr. A. Horowitz in preserving to highlight the important role of nutrition in health in poor countries.

diseases among women and children living in poverty. The interactions have been well described, in qualitative terms[1,2,3]. In general the more direct mechanisms are known -- described as the malnutrition-infection cycle[3] or spiral[4] B with effects through appetite, immunity[5], and integrity of epithelial tissues. A number of intervention trials in poor communities demonstrated an impact of improved diet on child mortality and morbidity (reviewed in[6]).

Malnutrition means non-optimal status of the individual with reference to one or a number of nutrients, including dietary energy. Nutrient deficiencies vary in their manifestations, some leading to specific clinical signs, many affecting growth at an early stage[7]. Those with distinct clinical signs and/or growth effects (e.g. iodine, iron, vitamin A, protein, energy) have historically received the most attention; those with less clear or non-specific signs (e.g. zinc) less so. Growth failure in particular has been widely used as a general measure of nutritional status, to the point that malnutrition has come to be almost synonymous with low anthropometric values, and nutritional status with anthropometry[8]. This has led to some misunderstandings, which need to be addressed in trying to estimate the contribution of nutrition to the global burden of disease.

In sum, while underweight (or stunting, especially in growing children) is a good indicator of many of the effects of the interaction between inadequate diet and infectious disease, it results almost always from a *combination* of diet and infection, operating cyclically. Intervention to interrupt the cycle (or spiral) is not necessarily nutritional in the sense of dietary, but may well include this. Second, the nutrition deficit is not necessarily energy (or protein -- which is used as energy when total energy intake is deficient). For example, deficiencies of other nutrients that increase sickness (almost all, through compromising immunity) and depress appetite will cause growth failure and/or wasting. Considerations such as these have led away from the term protein-energy malnutrition (PEM) towards general malnutrition, for which low anthropometry is the usual indicator, recognized as being non-specific as to cause. One cause will usually be infection, possibly as the major (or even only) cause[8,9].

Thus while low anthropometric values are good predictors of mortality and ill-health, this does not imply that a single dietary intervention is necessarily the best response. It is this concern that may account for the paradox of malnutrition being recognized as a major risk factor, without giving it the weight that this finding implies. An example is the estimate of the contribution of malnutrition to the burden of disease in developing countries as 18%, more than twice as much as the next ranked factors (poor water, sanitation, and hygiene)[10]; yet the article's discussion focuses on all risk factors *except* nutrition. The 18% contribution of malnutrition is based on estimates from an earlier draft of part of the work reported here[11].

The method of assigning components of the global burden of disease to specific causes, and estimating the effects as DALYs lost, was developed for the World Bank's World Development Report, entitled 'Investing in Health'[12]. The methods overall are described in a number of publications (e.g.[10]). The various estimates of the contribution of malnutrition refer mainly to direct effects, and concentrate on underweight and vitamin A. Since then two features have emerged. The first is the risk factor estimates themselves. Second are new estimates of the extent of micronutrient deficiencies[13], and assessments of the contribution of these as risk factors as well as directly causing ill-health. It was therefore thought useful to bring together the direct and risk factor (indirect) estimates of the contributions of the major known deficiencies: general malnutrition, as assessed by anthropometry, and deficiencies of vitamin A, iodine, and iron, as far as feasible disaggregating by region of the world and biological group.

There are difficulties in interpreting the implications of interactive factors, since they will not add to 100%. For example, removing either a pathogen or its vector can cause a 100% reduction in disease, but removing both does not lower it by 200%. With positive interactions (synergies) quite large attributable risks could be expected from single risk factors. Nutrients often interact and multiple deficiencies are likely to be common: a prevalence range of 13-27% of multiple deficiencies in pre-school children, depending on the assumptions used, was estimated as described in[13], table 10. Nonetheless, a first step is to assess the direct and indirect effects of the single nutritional deficiencies.

This paper brings together an updated version of an earlier report[11] which contributed to the estimates published by[14], for which low anthropometry was the only condition examined, with new calculations based on prevalence estimates of micronutrient deficiencies made for 'The Micronutrient Report'[13]. From these the contributions of malnutrition relating to protein-energy and to deficiencies of iodine, iron, and vitamin A to the global burden of disease have been estimated.

Methods

Low anthropometry in relation to mortality and morbidity

The work by Pelletier *et al*[15] based on eight prospective studies of anthropometry in young children in relation to mortality outcome demonstrated that this relation was logarithmic, hence interactive (log mortality by group was linear with z-score of weight-for-age, with a negative slope). These eight studies were not repeated, as once the relation was clear it would have been unethical to follow the children prospectively and not intervene; and eight are too few

to study any differences -- by region, age, disease pattern, and other such factors. However, a much larger number of cross-sectional surveys, and studies from clinic and hospital records, existed in the literature; these have somewhat greater problems of attribution of causality, but provide enough data to allow investigation of other factors, even if the conclusions are weaker.

Data were required which gave estimates of morbidity or mortality in one or more malnourished groups, compared with a better-nourished group. This allows the calculation of the relative risk of the particular measure of morbidity, or mortality, by change in nutritional status. The variables were: definition of risk group(s) versus comparison group, in terms of nutritional status; definition of outcome (mortality, measures of morbidity); outcome rate in risk group, and in comparison group. The ratio of these last two equals relative risk (RR). At the same time, a number of classifying variables were recorded, such as location, date of study, length of follow-up time, age group, source of information, etc.

Literature searches

A substantial body of literature had been compiled, up to 1989, for the ACC/SCN publication "Malnutrition and Infection", by Tomkins and Watson[3], which contains an abstract of each article. This was searched for data that would give relative risk estimates. For publications from1989 to 1997, literature searches were conducted on Medline, to extract citations likely to contain quantitative estimates of risk with respect to nutritional status. In addition, a review specifically on acute respiratory infections and nutrition, compiled by Victora *et al*[16] was extracted, having a number of useful references, including calculations of relative risk. The bibliography given by Pelletier *et al*,[15] was used to check for citations previously missed. The literature extracted is given in Annex 1; the median date of publication was 1989.

In setting up the database, a case was defined as one estimate of a relative risk of morbidity or mortality, from one or more bands of nutritional status in the risk group(s), compared to a well- (or better-) nourished comparison group. Most cases (180 out of 225) were simply a two-group-comparison, for example risk group defined as less than 80% weight for age, and a comparison group defined as more than 80% weight for age. In the other cases, the relative risk with the comparison group was separately assessed, for example less than 60% weight for age, 60-70% weight for age, and 70-80% weight for age, with greater than 80% weight for age as comparison group. These are treated as a single case, and the average slope of log relative risk vs SDs wt/age was estimated (by inspection).

Calculations

The relation between relative risk and nutrition status was taken as log-linear, in line with the findings of Pelletier *et al*[15]. Therefore the logarithm of the relative

risk (y-axis) was plotted against the indicator of nutritional status itself (linearly, x-axis). Where there were multiple nutritional status groups, this did appear to provide for a relatively good fit, certainly better than non-log - linear. A similar approach was taken with the usual case of just two groups. The interval in the two group situation was calculated by estimating the median values of the areas under the normal curve (i.e. the points at which the area was halved), for above and below the cut-point (usually -2SDs by NCHS references[17], but in some Asian cases as low as –4SDs) using a standard normal deviate calculation and then calculating the distance between these -- as shown in the illustration given in Figure 1. The mean of the distribution was estimated using the known average prevalences by region below -2SDs of NCHS reference standards (i.e. Asia 50%, Sub-Saharan Africa 30%, others 20%). This procedure gave estimates of the difference between two groups in wt/age z-score units, that is the interval between groups that then provides the denominator when calculating the log RR/SD; as examples, for wt/age above and below -2 SDs this interval was 1.7; for -4 SDs it was 2.8.

The slopes (log RR/SD) were then converted to the anti-log to give the factor by which the RR should be multiplied per SD of wt/age (or ht/age, etc) deficit, and this factor (multiplier in the tables) was used in the analyses reported below. From these procedures some 225 estimates were identified relating anthropometric measures with mortality or morbidity, distributed as shown in table 1. The additional variables coded and used in analysis were: age group, country, and follow-up time (between nutritional and outcome assessment).

The value of the multiplier (the factor by which risk was multiplied per SD of wt/age deficit) was constrained to be </= 4.0, to avoid a limited number of outliers having undue influence: 10 cases had multiplier values in the range of 4.2 to 9.4, seven of these from one study in Zaire. 19 cases had a factor value of < 1, but only three less than 0.85 (from Ethiopia, 0.59; China, 0.37; Yemen, 0.37) and these three were set to missing. This gave 206 plausible non-missing values of the multiplier factor.

This factor, as the relative risk between two groups of 1 SD separation, was converted to a relative risk for groups separated by 2 SDs, by raising to the power of 1.7 (which was the average interval between the <-2SDs and >-2SDS groups calculated as discussed earlier). We are excluding the risk for those at -1 to -2 SDs by selecting only the -2SDs group, making the estimates a recognized underestimate. (Also, only infectious diseases are included as discussed elsewhere in this paper, again leading to a conservative estimate.)

Converting this relative risk to the population attributable risk (PAR) uses the procedure and formula for estimating given by Pelletier *et al*[15] (page 2106S), and in standard text books (e.g.[13]), as follows :

PAR = (DALYs lost due to malnutrition)/(total DALYs)
= (Prevalence of malnutrition x (RR - 1))/(1 + (Prev. x (RR - 1))

The process is illustrated in table 2 with reference to India, for the age group zero to four years. The burden of disease estimates in terms of DALYs are distinguished as those related to premature mortality (years of life lost – YLL in[10]), and those due to morbidity (years of life with disability -- YLD). The disaggregated data can be found in[10]. Here the sexes are combined, and the column labeled “Both sexes, ages 0-4y” is thus the estimated lost DALYs from mortality and morbidity for both sexes, aged 0-4 yrs, broken down into the losses from (i) communicable, maternal and perinatal, (ii) noncommunicable diseases, and (iii) injuries. The effect of malnutrition is applied here only to the first category, which is infectious disease plus maternal and perinatal problems B the latter are also likely to be related to malnutrition in developing countries. While nutrition plays a role in noncommunicable disease, estimates relating to these are not made here.

The column labelled “Proportion underweight” in Table 2 shows the known prevalence of underweight (-2SDs) for zero to four year old children in India. The column labelled ‘Multiplier’ is the RR/SD. This is converted to “RR/1.7SDs” (the relative risk between the two groups above and below –2SDs) as described earlier, as (multiplier) 1.7. From this, the population attributable risk (PAR) is calculated according to the formula given above, in this case giving a value of 0.62. This is the proportion of the applicable burden -- that due to communicable, maternal and perinatal mortality -- that would be removed were there no malnutrition. Multiplying the original DALYs lost in this category (90,221,012) by 0.6189 gives the DALY loss due to malnutrition as 55,840,257. This reduction is subtracted from the total lost DALYs in this group (90,221,012), to give the figure for “DALYs remaining after eliminating malnutrition – Group I diseases” of 34,380,755 for mortality; this is the reduced DALY loss due to mortality calculated for the situation if there were no underweight. The DALYs from malnutrition are also subtracted from the overall mortality DALYs (groups I, II, & III), to give 52,266,411, which represents a 51.65% reduction in the overall mortality burden in this group; this is the figure used to add with morbidity, and across regions.

A similar calculation is done for morbidity, substituting the new factor (RR/SD deficit, or multiplier) of 1.405, which gives the slope per1.7 Sds (the estimated interval for 2 groups </> -2SDs) as (1.405)1.7, = 1.783, i.e. the relative risk between the two groups. The PAR (0.32) is calculated from this RR and the

prevalence using the formula given above. The DALYs from malnutrition in this case are less, (2,437,398 DALYs), due the lower PAR and smaller burden of morbidity compared to mortality. The reduction is 8.55% of the total morbidity burden.

The calculation for all regions (as defined by the World Bank[12]) repeated this process. The average prevalence of underweight (<-2SDs) in children 0-5 years by region was applied, derived from[9], ignoring the slight difference in prevalence due to the age group in the present calculations being 0-4 years. The original estimates of DALY loss were taken from Murray & Lopez[10]. While the factors were applied only to group I diseases (communicable, maternal, and perinatal), the reductions in the disease burden are also calculated with respect to the DALY-loss from *all* causes, for the age group (i.e. using all-cause burden as the denominator).

Vitamin A deficiency and mortality

The estimates of Beaton and co-workers[19] of the expected reduction in mortality from preventing vitamin A deficiency formed the basis for calculating the indirect effect on disease burden through mortality in children of < 5 yrs: they calculated the average reduction in mortality, from 8 trials, as 23%, vitamin A having a protective effect with relative risk of 0.77. Some crucial considerations in applying this value were, it should be noted, not answerable by the meta-analysis of Beaton *et al*[19]. First, the age range to which the estimate applies was 6 to 60 months, and the applicability from birth to 6 months was not known: 'At this time, we are unable to reach a firm conclusion about short and long-term benefits of vitamin A supplementation to infants under 6 months of age' (p xii). Given that breastfeeding is the main way in which infants under 6 months would be protected, that maternal supplementation is an intervention of choice, and that recent opinion is that vitamin A deficiency is likely to have a similar relation at < 6 months[20], here the same value is applied from birth (to do otherwise would be complicated as DALY values are given for the 0-4 age group). However since most infant mortality is in the first few weeks, this is an important assumption.

Second, the relation of the mortality effect to the extent and severity of the deficiency was not known from the Beaton et al studies[19]: We note the very important caveat that we were unable to address a critically important question, in the presence of biochemical evidence of vitamin A depletion, without evidence of actual xerophthalmia in the population, is vitamin A supplementation likely to have an effect on mortality? (p.53). Clearly we could not apply the same relative risk estimate to all populations -- with no deficiency there would be no effect -- so some assumptions were needed. We based these on the observed scatter of points relating RR to xerophthalmia prevalences, as shown in figure

5.5 of Beaton *et al*[19] (p.53). We assumed an estimate of 1.0 for the RR at zero prevalence of xerophthalmia and that the risk then increased linearly up to a prevalence of 1%, to an RR of 0.77, remaining at 0.77 thereafter. The RR averaging 0.77 in the calculations of Beaton *et al*[19] was for the treatment group/comparison group B i.e. the protective effect of vitamin A capsules (VAC). It is generally assumed that this represents the effect of vitamin A deficiency (VAD) on mortality, that is that the VAC-plus group was not deficient. Here the inverse relation is required, i.e. the effect of deficiency on mortality, which is 1/0.77 = 1.30. The algorithm for interpolating this relative risk (RR2) from 1.0 at zero prevalence of clinical VAD to 1.30 at 1% VAD prevalence is RR2 = (1.0 + (0.3 * % prevalence)). The response to reducing VAD is taken (by Beaton *et al*[19], p.53, and by conventional wisdom) to apply to the whole population in which clinical VAD is seen. In the PAR calculation for VAD/mortality, the prevalence is thus taken as 1%, and the equation is:

PAR = (Deaths due to VAD)/(total deaths) = (1.0. x (RR - 1))/(1 + (1.0. x (RR - 1))

Clearly a major unknown concerns what proportion of the population benefits to this extent of risk reduction; this is partly addressed by reducing the RR applied when the VAD prevalence is less than 1%.

Estimates of clinical vitamin A deficiency by country (approximating to the active xerophthalmia at baseline in table 5 of Beaton *et al*[19] and to WHO definitions) were taken from those calculated for The Micronutrient Report (Mason *et al*[13]), as described there (pp.15-16), for 1995. Given the decline in clinical VAD this makes the estimate conservative for 1990, the base year for the DALY estimates. The average RR estimates by region, derived from the national clinical VAD prevalence estimates, were: India, 1.30; China, 1.06; other Asia, 1.17; Sub-Saharan Africa, 1.21; Latin America and Caribbean, 1.07; Near East/North Africa, 1.09. These factors were applied to the DALY loss estimates for the age group 0-4 years from infectious disease mortality, in a manner analogous to that shown for underweight in India in table 1.

Vitamin A direct effects

For the direct effects B that is the disability caused by vitamin A deficiency *per se* B the estimate used by the World Bank/WHO in the 1993/4 publications[10,12] was of 11.8 million DALYs lost, all in 0-4 year old children. This is approximately in line with results calculated from current prevalence estimates of sub-clinical VAD, of about 140 million children affected in 1995 ([13] p.32). Supposing a

[c]Degrees of disability are ascribed as a factor applied to the time disabled B e.g. a year with the least level (factor of .096) is counted as 0.096 DALYs lost. This level is defined as limited ability to perform at least one activity in one of the following areas: recreation, education, procreation, and occupation.[10]

minimal level of disability (say 0.096, following [10]p.12[c]) gives 13 million DALYs lost from sub-clinical VAD. Clinical deficiency affects some 3.3 million (in 1995, [13] table 6), for which a disability factor of 0.4 seems correct (class 3, 'limited ability to perform activities in at least two of: recreation, education, procreation or occupation' [10] p.12); this indicates that clinical VAD makes a relatively minor direct contribution, of 1.32 million DALYs in this calculation. The original estimates as given by [10](Annex tables 1-12, pp. 109-138) of direct effects of VAD in terms of DALY loss, total and by region, are therefore retained here, amounting to 11.8 million lost DALYs overall (see table 10 discussed later).

Severe anemia and maternal mortality

Iron deficiency, which is a major cause of anemia, is likely to increase risk of disability and death particularly among reproductive age women and infants and young children. However, quantifying this risk for the different vulnerable groups would be an extensive task, and it was decided to focus where the risks were fairly clear and accepted, and some data had been compiled B on maternal mortality risk in pregnancy in relation to severe anemia, which is likely to constitute one of the most important consequences.

In a review of anemia and pregnancy at a recent workshop, it was concluded that while the relation of mild/moderate anemia to mortality was unclear, nonetheless, the relationship of maternal mortality to severe anemia (Hb < 70 or 80 g/L) was remarkably consistent: severe anemia was associated with about a fourfold increase in death[21]. Nine studies are listed showing a range of results (table 1 in the report), and by inspection it seemed that taking an RR of 4.0 relating severe anemia to maternal mortality rate (MMR) would indeed be justifiable in making some approximations of the contribution. A similar value was estimated[22] for severe anemia and maternal mortality (RR = 3.5, but with a lower cut-off for severe anemia of 47 g/dl). The results given by Murray & Lopez[10] include maternal deaths by region, DALYs for morbidity (YLL), and the total DALYs (from which DALYs from mortality (YLD) can be calculated by difference). These are also broken down into causes (haemorrhage, sepsis, eclampsia, hypertension, obstructed labour, abortion). As the estimated RR of 4 for severe anemia is for all causes (not only haemorrhage), it is not clear whether to apply this to all maternal deaths or only to that proportion in which haemorrhage is the cause; both were calculated here, using the same PAR.

Prevalences of anemia at national level are not available for all countries, but estimates have been made at regional level ([13] p.29), and available national data on anemia in women (pregnant, prevalences < 11 g/dl, and non-pregnant, < 12 g/dl, ages 15-49 years) have been compiled ([13]Appendices 4 &5). Of the total of 432 datapoints (including sub-national), some 25 had prevalence estimates

for *both* < 11 g/dl and < 8 g/dl (omitting values above 60% prevalence of Hb < 11). The relationship was used to estimate the prevalence of severe anemia (< 8 g/dl) from the previously estimated prevalence of mild anemia in pregnant women (Hb < 11 g/dl; [13] p.29). The regression equation was:

> Prevalence < 8 g/dl Hb = 0.399 + 0.0926 (Prevalence < 11 g/dl Hb)
> (n = 25, Adj R sq = 0.473, for coefficient p = 0.000).

From this, the prevalence by region of severe anemia was estimated, and a relative risk of 4.0 applied as:

(DALYs lost due to severe anemia from maternal conditions/Total DALYs lost from maternal conditions) = (Prev severe anemia x (4.0 - 1))/(1 + (Prev severe anemia x (4.0 - 1)))

Two scenarios were calculated, to bracket the likely effect with high and low estimates: (a) applying the calculation to the total maternal *mortality plus morbidity*; and (b) applying it only to maternal *mortality* associated with haemorrhage. This was indicated also because the contribution of anemia to the morbidity from haemorrhage is not known.

The direct estimates of anemia burden are 13,896,000 DALYs lost world wide, in Murray & Lopez 10 p.137. The extent of disability from mild anemia (e.g. < 12 g/dl Hb in non-pregnant women, < 11 g/dl Hb in pregnant women) is not well quantified. If we just take reproductive age women, about 530 million are affected in the developing world[13] (p.35),[23], at a disability class I (0.096) this gives about 50,000,000 DALYs lost, substantially higher than the estimate of 13,896,000 for all people. This figure of 50,000,000 DALYs is used below.

Iodine deficiency disorders

The indirect effects of iodine deficiency have rarely been quantified. Two studies have estimated effects on infant mortality of iodine treatment in deficient areas, in Indonesia[24] and China[25]. These both found large protective effects of iodine on infant mortality, which as for vitamin A supplementation can be inverted to estimate the risk from iodine deficiency. Thus the results of Cobra *et al*[24], of RRs from 0.20 at 1 month, 0.30 at 2 months, and 0.52 at 4 months, translate to IDD having RRs of 5.0 to 1.92. The study in China used iodination of irrigation water for a 2-4 week period, then followed changes in IMR over 2-3 years. The reduction in IMR was dramatic, with an odds ratio of 0.43, translating approximately into an RR of 2.3 for IDD on IMR. The area in China was severely iodine deficient (e.g. median urinary iodine < 10 mcg/l before treatment); in Indonesia however the goitre rate was not particularly high at around 10% ([24], table 1).

It is difficult to know how to use these two results. On the one hand, a general halving (say) of the IMR with increased iodine intake seems unlikely, as the IMR has not been observed to plummet to this extent with the rapid adoption of iodized salt, now reaching about 65% of households in developing countries, up from about 10% in the 1980's. On the other hand, it seems useful to calculate at least roughly the possible effect in iodine deficient areas. This was done at regional level (as national IDD estimates are not consistently available). To be conservative, it was assumed that the RR for infant and child mortality (for group I DALYs: communicable diseases, maternal and perinatal causes) was 2.0, and that this applied to those with IDD, using the population goiter rate ([26,13] p.34), rounded to: India, 10%; China, 10%; other Asia, 20%; Sub-Saharan Africa, 15%; Latin America/Caribbean, 10%; Middle Eastern Crescent, 20%. The formula is:

(DALYs lost due to iodine deficiency in 0-4 yr children/ Total DALYs lost in this group) = (Prev goiter in population x (2.0 - 1))/(1 + (Prev goiter in population x (2.0 - 1)))

The direct effects of iodine deficiency were estimated by Murray & Lopez ([10] p.137) as 7,214,000 DALYs lost worldwide. The recent estimates are of 655 million people with goiter[26]; applying the lowest disability value of 0.096, this gives 62,880,000 DALYs lost. Given that disability in terms of lowered productivity and IQ is well established[27,28], at least the lowest disability class (limited ability to perform at least one activity ...; see footnote c) would seem to be applicable. The 7.2 million DALYs appears to be an underestimate, and for our calculations, the value of 60 million is substituted.

Results

Contribution of underweight to mortality and morbidity in 0-4 yr children

The mean values representing the factor by which the risk of mortality increases per SD of wt/age deficit (called the mortality risk multiplier) are shown in table 3. The regions with reasonable sample size were India, other Asia, and Sub-Saharan Africa, which are also those with the major problems. The multiplier means were significantly different from 1.00, as shown by the 95% confidence intervals (mean +/- 2 SEMs), averaging 2.25 overall, from 50 results. They did not differ significantly by region (note that only 2 cases were available for Latin America and Caribbean, both from Brazil). For comparison with our mean of 2.25, the equivalent mean values implied by the slope of -0.0264 per percentage point of wt/age from the eight studies analyzed by Pelletier *et al* ([15] p.2110S) is 1.84. (Separating out the results used by Pelletier *et al*, in our calculations, which used a slightly different procedure we made the mean 2.15 (1.64 - 2.66), not significantly different from the other results in our data.)

We conclude that the estimates here, from a larger number of (less powerful) studies, are in line with the estimates of Pelletier *et al*[15].

The mortality risk multipliers were examined for association with other factors retrieved from the original study results: age of child (range, mean), length of follow up, disease (diarrhea or ARI, where available), population (national) underweight prevalence, and IMR. Neither age nor follow up time were significantly associated, and there were insufficient data points to assess the effects of diarrhea vs ARI as cause of death (multiplier = 2.90 for ARI (n=9), 1.52 for diarrhea (n=3)). The population underweight prevalence was not related. The only factor examined which was associated at all was the underlying IMR, which showed a negative association with a p-value of 0.12 (n=50); if real, this implies that the effect of underweight as a risk factor is *greater* when the underlying IMR is *lower.*

To calculate the PAR, the regional mean values of the risk multipliers were used for India, other Asia, and Sub-Saharan Africa, as shown in table 3. For the other regions (China, Latin America and Caribbean, and Middle Eastern Crescent) only 3 estimates in total for mortality were available, so the overall mean was instead applied. The PAR was calculated for the group defined as less than -2SDs wt/age, as the common definition of underweight[29]. Increased risk above this cut-off was not assessed. Since the multiplier is per SD deficit, it was raised to the power of 1.7 (the mean interval) to calculate the PARs used here, equivalent to above/below -2 Sds. The results are shown combined with morbidity as discussed later in table 5.

The equivalent results for morbidity are shown in table 4. Here, they are distinguished by disease where this was reported, as ARI or diarrhea. There is some tendency for underweight to be more predictive of ARI morbidity than for diarrhea, as seen comparing the multiplier values overall of 1.435 for ARI and 1.234 for diarrhea. The multiplier values were much smaller than for mortality B the risk of morbidity increased to a lesser extent with increasing weight deficit B but in most cases were still significantly greater than 1.00. For table 5, regional means of multipliers were used for India, Sub-Saharan Africa, and Latin America and Caribbean; for other Asia, China, and Middle Eastern Crescent the overall mean was applied, due to limited data for these regions specifically.

The results from applying the population attributable risk (PAR) to the estimates of disease burden (DALY-loss) by region, for mortality and morbidity, are shown in table 5. The overall reduction in the age-group 0-4 years is estimated as 31%, if underweight were eliminated. The largest reductions, it is calculated, would be from improvements in infant and child mortality in India and Sub-Saharan Africa (52% and 45%). In all cases a greater impact on mortality

than morbidity is predicted. This stems both from the higher RR of mortality from underweight, and from the relatively greater contribution of mortality to the burden in these regions for this age group.

Predictive value of other anthropometric indicators

The relation of ht/age and wt/ht with mortality and morbidity outcomes was calculated analogously to wt/age, and the results are shown in table 6. Wt/age and wt/ht appeared to behave similarly, with ht/age having slightly less predictive power, although the differences were not significant. These results were not altered by controlling for follow up period, although the sample size was perhaps too small for this to be effective. This demonstrates that wt/age is as good as or better than the other possible indicators studied for identifying health risks.

Contribution of vitamin A deficiency to mortality in 0-4 yr children

It was assumed (see Methods section) there is an association of mortality with VAD throughout populations in which clinical VAD exists, approximated by setting the RR to 1.00 at zero prevalence and raising it to1.3 at 1% prevalence, then keeping it at that value. This RR is applied to the whole population, in line with the conclusions of Beaton *et al*[19], and with the calculations underlying the World Bank estimates[12] . The results are shown in table 7. These were calculated country-by-country then summed, as the non-linear association would have given somewhat different results directly calculated from aggregate regional figures. Nonetheless, the expected reduction in disease burden is closely related to the regional prevalence. A further assumption is that the mortality reduction would apply to infants of less than 6 months B which is likely, but more closely related to maternal nutrition (and intervention) than for older children.

Again, the largest effects would be expected in Asia and Sub-Saharan Africa. Between 12% and 19% reduction of mortality from all causes in 0-4 year old children should result from eliminating VAD. A total of 13% of the 0-4 all-cause mortality is predicted. This overlaps with underweight in the sense that most VAD children are also underweight. However, VAD has only a minor effect on underweight[30,31], moreover the mechanisms are likely to be different. Thus this reduction should in principle be additive to that expected from underweight reduction.

Severe anemia as a risk factor for maternal conditions

Using the approach described in the Methods section, applying a RR of 4.0 for severe anemia with maternal mortality and morbidity, gives the results shown in table 8. This attempts to bound the effect, by applying the reduction expected

from eliminating severe anemia to either the total maternal mortality plus morbidity, or to the maternal mortality only associated with haemorrhage. (The other conditions included for maternal morbidity and mortality are sepsis, eclampsia, hypertension, obstructed labor, and abortion.) In table 8, the higher reduction, totalling 12.6% of maternal conditions DALYs, applies this to overall maternal morbidity and mortality; the lower figure is derived from only maternal mortality. The total DALYs saved are about 3,600,000; only a fraction of those in young children from VAD (55,000,000 B table 7) or underweight (169,000,000 B table 5).

Applying the average PAR (0.1256) to the estimated maternal mortality figure of 427,700 deaths/year indicates that 53,700 deaths per year would be averted by preventing severe anemia.

Anemia as disease

Anemia is the most extensive known deficiency, with prevalences of over 50% for mild forms in poor countries for the most vulnerable groups, reproductive age women and young children. While the extent of disability associated with mild anemia is unsure, it was suggested in the methods section that at least for reproductive age women it should be counted as class I, assigned a weight of 0.096. This adds a further 50,000,000 DALYs to the burden from anemia in the developing world, and implies that for this deficiency the direct effects may be much more important than those as a risk factor for other conditions.

Iodine deficiency disorders

The effects of iodine deficiency as a risk factor are hardly known, and as discussed in Methods, calculations here are only illustrative. A somewhat conservative estimate, applying a RR of 2 for infant and child mortality only to the population proportion with goiter, gave the figures in table 9. By this calculation, around 10% of child mortality DALYs lost would be saved, amounting to some 44,000,000 DALYs. While it has recently been seen that mild iodine deficiency may contribute to underweight[32], the mechanism by which iodine is protective is unlikely to involve growth directly, so this too is primarily a pathway that does not overlap with underweight B that has its effect largely independently of underweight.

As noted in Methods, the previous estimates ([12], p.137) of the direct effects of IDD seem likely to be an underestimate, now that it is known that some 650 million people are affected; thus we use a value of at least 60,000,000 DALYs for the direct effects (an increase of 52,000,000 over the previous estimates).

Combining risk factor and direct contributions of nutritional deficiencies

Underweight remains the largest nutritional contributor to child mortality and morbidity, according to these calculations, but iodine deficiency and VAD together are of a similar magnitude. The results are brought together in table 10. Major groups affected by malnutrition have been assessed, but no assignment of nutrition as a risk factor has been made outside the groups of 0-4 yr old children, and reproductive age women for anemia. The assessment is incomplete and thus likely to be an underestimate.

For the direct effects, new and higher estimates are suggested for IDD and iron deficiency: both these have been more clearly recognized since the previous calculations for the World Bank/WHO publications[10,12]. Increasing these estimates (in table 10) raises the direct effects of malnutrition. However, this study was aimed primarily at assessing the indirect, risk factor effects, and the major point is that this indirect contribution is very significant. As shown in table 10 and illustrated in figure 2, while nearly 30% of the global disease burden could be removed by eliminating malnutrition, the major part amounting to 20% would come from the indirect risk factor effects.

Finally, the results in terms of percent reduction in the DALY-loss of each group by condition (e.g. underweight for 0-4 year old children, as given in the last column of table 10) are broken down by geographic region, in table 11. In each cell this gives the % reduction within the group, then the total DALY-loss reduction, then (in the third line) expresses this as a % of the total (all causes, all groups, all developing countries) DALY-loss. For example (reading the first line in each cell) the potential reduction from eliminating underweight is highest in India (at 46.6%) and least in Latin America and Caribbean (16.8%), averaging 35.0%. Potential benefits from addressing other deficiencies vary by region - for instance iron deficiency anemia is of high potential in the Middle Eastern Crescent, and Asia. Looking at the priorities indicated within geographic areas (reading the table horizontally), while underweight in children is seen from this perspective to offer the largest benefits in India and Sub-Saharan Africa, anemia is highlighted in China and other Asia (S and SE Asia without India and China). Eliminating vitamin A deficiency in children is generally seen to offer around half the potential benefit of eliminating underweight, but may well be considerably easier.

Using the % of the total (all cause, all groups, all developing countries) burden, the results in table 11 (third line in each cell) show the distribution of the estimated 32.4% benefit to be gained from eliminating malnutrition (for the conditions assessed). This takes account of the populations of the different regions, in contrast to the estimates by group. About half of this, 14.95% of the

total burden, would come from eliminating underweight; about 5% of the total burden from underweight in India and Sub-Saharan Africa. Vitamin A deficiency is similarly most significant in India and Sub-Saharan Africa, with iron and iodine deficiencies more evenly distributed geographically.

Discussion

Improving nutrition would have broad and generally non-specific (or multi-purpose) benefits in reducing the effects of infectious diseases. Non-specific public health measures tend to be underestimated in their impact[33], as the benefits are spread among so many conditions. The estimates here try to capture this broad effect, using underweight (itself a non-specific measure[8]) as an indicator of inadequate nutritional status, in part at least caused by inadequate diet.

It should be stressed that the results using underweight *do* imply that if underweight were removed the burden of disease would be substantially reduced B by about 20% in children in developing countries B but do not imply *how* that reduction should be achieved. We know that control of infectious disease will increase growth in children and reduce underweight B improving nutritional status through a number of mechanisms including increased appetite, reduction in nutrient losses, and so on. Put otherwise, growth and nutritional status will benefit from reducing the malnutrition-infection cycle, and there are several ways in which the interaction between nutrition and infection can be interrupted. Improving nutrition does not *always* require a dietary intervention; but better diets may often be crucial to improving health.

Assessing nutrition as a risk factor B measured as underweight in this example B provides policy guidance in stressing that interventions that will reduce malnutrition will be effective in reducing disease burden, and gives some quantification to this. There are strategies with costs attached for improving nutrition (measured by reducing underweight) by anticipated amounts[34,35], and these could be linked to disease burden reduction. In general, successful strategies for reducing malnutrition involve community-based and service delivery programs aimed at general malnutrition, with specific micronutrient deficiency control programs that have both vertical and local components.

For two of the conditions included, vitamin A deficiency (VAD) and iodine deficiency disorders (IDDs) there are direct interventions of likely (VAD) or proven (IDD) effectiveness: vitamin A supplementation and salt iodization. These are now covering large proportions of the vulnerable populations, and can be expected through both direct and indirect effects to be reducing the disease burden by a substantial amount (table 10), moreover one which can be pre-

dicted if the calculations presented here are valid. Sustaining and ensuring full coverage and effectiveness of these programs, and moving towards wider use of fortification in the case of vitamin A, would have considerable impact on the burden of disease.

For iron deficiency, the estimate here is that much of the effect on disease burden is direct, through the disability caused by anemia; and that this may have been underestimated in earlier calculations. For many of the most affected populations, rice is the staple food which cannot yet be effectively fortified: investment in research and then implementation of iron fortification in these populations B of rice itself, or other suitable commodities B would have great pay-off in terms of reduced disease burden. Reducing severe anemia and thereby avoiding maternal mortality could save many thousands of lives.

These calculations, as summarized in tables 10 and 11, have not attempted to estimate the contribution of malnutrition to disease burden for all population groups B in fact only for a minority. The results apply to children of 0-4 years, and for iron to reproductive age women. No estimate has been made for other groups, since the relationships are not known, as well as for economy of effort. Our previous estimates extrapolated the factors determined for young children to other age groups B which has some logic, as there is certainly some effect -- but this is discontinued here. These previous results were the basis for the estimate of 18% of developing country DALYs attributable to malnutrition given by Murray and Lopez[14] table 5. This 18% did not include micronutrient deficiencies, being based only on the underweight estimates. Here, we have confined the estimates to young children and reproductive age women, not ascribing any risk to malnutrition in other groups. Thus we have reduced the extent of populations assessed, and increased the number of nutritional conditions considered. This is in part to be conservative, partly because of lack of data. We also have not included any estimates of the effects of nutrition on chronic disease, either concurrent (e.g. with obesity) or through intra-uterine effects manifesting later in life[36,37].

While these more selective results may fit less neatly into a presentation of the global DALYs attributable to malnutrition, they do focus on known priorities. The overall figure (bottom row, tables 10 and 11) comes out approximately as 30% of DALYs attributable to malnutrition, 20% as a risk factor and 10% as direct effects. However, contributions within groups (biological and by region) are perhaps more useful. Overall, the results reinforce the case that Sub-Saharan Africa and Asia (especially South Asia) have the greatest needs. The effects of malnutrition, particularly as a risk factor, are very extensive, implying large potential benefits to health from addressing malnutrition. More attention to public nutrition could be the most effective investment in preventing ill-health and premature mortality throughout much of the developing world.

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Figure 1 Illustration of calculation of interval distance between two groups above and below cut-off (e.g. > & < -2SDs).

Figure 2 Contributions of malnutrition to the burden of disease, as % of burden that would be removed by eliminating different forms of malnutrition in the groups indicated.

Table 1

Distribution of cases identified and extracted from literature search and other sources, relating nutritional indices to outcome (mortality or morbidity).

Outcome	Disease	Nutrition index						
		Wt/age	Ht/age	Wt/ht	Birth weight*	Kwash -iorkor	Arm circum-ference	Total
Morbidity	Acute respiratory infections	6	-	9	7	-	2	24
	Diarrhea	42	14	15	-		2	72
	Unspecified	6	4	2	2	-	-	14
	Total	54	18	26	9		4	111
Mortality	All causes	43	24	24	8	11	4	114
Overall total		97	42	50	17	11	8	225

* Birth weight was combined with wt/age in most analyses.

Table 2

Example of calculation of reduction in disease burden (DALY-loss) from eliminating underweight in children.

	Both sexes, all ages	Both sexes, ages 0-4 y	Proportion under-weight	Multiplier	RR/ 1.7SDs	Population attributable risk (PAR)	DALYs from malnutrition	DALYs remaining after eliminating malnutrition		% reduct-ion
								Group I diseases	All causes	
India : DALYs from mortality										
All causes	200,575,462	108,106,668							52,266,411	51.7%
I. Communicable, maternal, perinatal	123,488,954	90,221,012	0.5900	2.1770	3.7528	0.61893	55,840,257	34,380,755		
II. Noncommunicable	60,417,159	15,083,564								
III. Injuries	16,669,350	2,802,092								
India: DALYs from morbidity										
All causes	92,070,432	28,493,878							26,056,480	8.6%
I. Communicable, maternal, perinatal	24,787,617	7,716,305	0.5900	1.4050	1.7826	0.31588	2,437,398	5,278,907		
II. Noncommunicable	57,225,268	17,642,778								
III. Injuries	10,057,547	3,134,795								
Total/average	292,645,894	136,600,546					58,277,655			42.7%

Table 3

Estimates of mortality risk multiplier (by which mortality risk is multiplied per SD of wt/age deficit) by region.

Region	Mortality risk multiplier per SD wt/age			RR comparing above and below - 2SDs wt/age
	Mean	No. of estimates	95% confidence limits	
India	2.177	10	1.645 - 2.709	3.75
China	-	-	-	-
Other Asia	2.123	22	1.819 - 2.426	3.59
Sub-Saharan Africa	2.319	15	1.841 - 2.796	4.18
Latin America & Caribbean	3.758	2	2.743 - 4.775	9.49
Middle Eastern Crescent	1.610	1	-	2.24
Total/average	2.252	50	2.014 - 2.490	3.97

Differences between mortality risk multipliers, P = 0.113, (F=1.99) overall; for three main groups (India, other Asia, Sub-Saharan Africa, P= 0.77 (F=0.270).

Table 4

Estimates of morbidity risk multiplier (by which morbidity risk is multiplied per SD of wt/age deficit) by region.

Region	Morbidity risk multiplier per SD wt/age			RR comparing above and below - 2SDs wt/age
	Mean	No. of estimates	95% confidence limits	
India: total	1.405	12	1.088 - 1.722	1.781
ARI	1.641	4	0.784 - 2.498	2.321
Diarrhea	1.323	6	1.021 - 1.624	1.609
Unspecified	1.179	2	-	1.323
China: ARI	1.489	1	-	1.968
Other Asia: total	1.124	17	1.034 - 1.214	1.220
Diarrhea	1.124	17	1.034 - 1.214	1.220
Sub-Saharan Africa: total	1.339	14	1.164 - 1.514	1.643
ARI	1.442	2	-	1.864
Diarrhea	1.385	10	1.160 - 1.608	1.739
Unspecified	1.011	2	-	1.019
Latin America & Caribbean: total	1.434	18	1.221 - 1.646	1.845
ARI	1.287	6	1.074 - 1.500	1.536
Diarrhea	1.214	8	1.116 - 1.311	1.739
Unspecified	2.095	4	1.607 - 2.582	3.515
Total	1.323	62	1.221 - 1.424	1.609
ARI	1.435	13	1.164 - 1.706	1.848
Diarrhea	1.234	41	1.149 - 1.319	1.430
Unspecified	1.595	8	1.147 - 2.043	2.212

For total, comparing ARI and diarrhea, $p=0.064$, $F=3.56$.
For no other differences is $p < 0.1$.

Table 5

Overall reduction in disease burden from eliminating underweight in 0-4 yr old children, by region.

	Both sexes, 0-4 y	Proportiion under weight	Multiplier	RR/1.7SDs	PAR	DALYs from malnutrition	DALYs remaining after eliminating underweight		% reduction
							Group 1 diseases	all causes	
India: DALYs from mortality									
All causes	108,106,668							52,266,411	51.65%
I. Comm.	90,221,012	0.5900	2.1770	3.7528	0.61893	55,840,257	34,380,755		
India: DALYs from morbidity									
All causes	28,493,878							26,056,480	8.55%
I. Communicable,	7,716,305	0.5900	1.4050	1.7826	0.31588	2,437,398	5,278,907		
China: DALYs from mortality									
All causes	35,277,161							26,005,672	26.28%
I. Communicable,	23,435,979	0.2200	2.2520	3.9753	0.39561	9,271,489	14,164,490		
China: DALYs from morbidity									
All causes	14,314,863							14,074,172	1.68%
I. Communicable,	2,036,113	0.22	1.323	1.6094	0.11821	240,691	1,795,422		
Asia other: DALYs from mortality									
All causes	53,629,202							32,935,919	38.59%
I. Communicable,	46,407,277	0.31	2.123	3.5960	0.44591	20,693,284	25,713,993		
Asia other: DALYs from morbidity									
All causes	13,171,456							12,642,906	4.01%
I. Communicable,	3,332,892	0.31	1.323	1.6094	0.15889	529,551	2,803,341		
SS Africa : DALYs from mortality									
All causes	133,369,079							73,759,608	44.70%
I. Communicable, maternal, perinatal	122,124,409	0.3	2.319	4.1784	0.4881	59,609,471	62,514,938		
SS Africa : DALYs from morbidity									
All causes	23,462,714							21,793,144	7.12%
I. Communicable, maternal, perinatal	10,330,311	0.3	1.339	1.6426	0.16162	1,669,570	8,660,741		
L Am Ca: DALYs from mortality									
All causes	23,316,124							18,964,750	18.66%
I. Communicable,	18,976,535	0.1	2.252	3.9753	0.2293	4,351,375	14,625,160		
L Am Ca: DALYs from morbidity									
All causes	9,083,754							8,821,188	2.89%
I. Communicable,	3,363,754	0.1	1.434	1.8456	0.07797	262,257	3,101,497		
MEC:DALYs from mortality									
All causes	60,705,419							46,404,591	23.56%
I. Communicable,	51,274,604	0.13	2.252	3.9753	0.27891	14,300,872	36,973,732		
MEC: DALYs from morbidity									
All causes	13,476,696							13,192,019	2.11%
I. Communicable	3,878,370	0.13	1.323	1.6094	0.0734	284,678	3,593,692		
Total/average								346,916,860	31.02%

Table 6

Comparison of different anthropometric indicators in relation to mortality and morbidity risk multipliers.

	Mortality			Morbidity		
	Mean multiplier value	No. of observations	Relative Risk [2]	Mean multiplier value	No. of observations	Relative Risk [2]
Wt/age [1]	2.252	50	3.98	1.323	62	1.61
Ht/age	1.929	23	3.05	1.114	18	1.20
Wt/ht	2.108	22	3.55	1.353	25	1.67

1 includes low birth weight, n = 17

2 between groups defined as less than and greater than -2SDs by NCHS/WHO standards, for each index (WHO, 1986 [29]).

Table 7

Reduction in disease burden from eliminating vitamin A deficiency (VAD) in 0-4 yr old children, through reduced mortality risk only, by region.

Region	DALYs lost from		Prevalence of clinical VAD(%)	Relative Risk	Population Attributable Risk	DALYs lost from VAD	DALYs remaining after eliminating VAD	% reduction	
	all causes	Group 1 diseases						Group 1 diseases	all causes
India	108,106,668	90,221,012	1.00	1.3000	0.2308	20,820,234	69,400,778	23.08%	19.26%
China	35,277,161	23,435,979	0.20	1.0600	0.0566	1,326,565	22,109,414	5.66%	3.76%
Other Asia	53,629,202	46,407,277	0.76	1.1711	0.1461	6,552,743	39,854,534	14.12%	12.22%
SS Africa	133,369,079	122,124,409	0.93	1.2102	0.1737	20,793,185	101,306,799	17.03%	15.59%
LAmCa	23,316,124	18,976,535	0.25	1.0680	0.0637	1,165,107	17,809,531	6.14%	5.00%
MEC	60,705,419	51,274,604	0.28	1.0930	0.0851	4,095,501	47,184,230	7.99%	6.75%
Total	414,403,653	352,439,816				54,753,335	297,665,286	15.54%	13.21%

Table 8

Reduction in disease burden from eliminating severe anemia in pregnant women, calculated in relation to (a) reduction in total maternal mortality plus morbidity; and (b) mortality associated with haemorrhage.

	Deaths	DALYs lost (thousands)			Anemia prevalence %		Population Attributable Risk	DALYs lost from anemia	DALYs remaining after eliminating anemia	% reduction
	(thousands)	from morbidity	from mortality	Total	Hb < 11 g/dl	Hb < 8 g/dl				
India										
Maternal total	129.4	3,998	3,826	7,824	53.90	5.58	0.14349	1,123,000	6,701	14.35%
Haemorrhage	38.8	217	1,148	1,365			0.14349	165,000	983	2.11%
China										
Maternal total	29.3	1,631	864	2,495	30.30	3.31	0.09043	226,000	2,269	9.04%
Haemorrhage	14.4	217	423	640			0.09043	38,000	385	1.53%
Asia other										
Maternal total	67.3	2,401	1,956	4,357	52.70	5.47	0.14094	614,000	3,743	14.09%
Haemorrhage	20.2	162	587	749			0.14094	83,000	504	1.90%
SS Africa										
Maternal total	137.2	3,916	4,076	7,992	48.50	5.06	0.1319	1,054,000	6,938	13.19%
Haemorrhage	41.2	207	1,223	1,430			0.1319	161,000	1,062	2.02%
L Am Ca										
Maternal total	23.8	1,092	708	1,800	31.00	3.38	0.09209	166,000	1,634	9.21%
Haemorrhage	4.8	109	141	250			0.09209	13,000	128	0.72%
MEC										
Maternal total	40.7	3,000	1,208	4,208	34.10	3.68	0.09941	418,000	3,790	9.94%
Haemorrhage	10.2	169	302	471			0.09941	30,000	272	0.71%
Total/average										
Maternal total	427.7	16,038	12,638	28,676			0.1256	3,601,000	25,075,000	12.56%
Haemorrhage	129.6	1,081	3,824	4,905				490,000	3,334,000	1.71%

Table 9

Reduction in disease burden from eliminating iodine deficiency (IDDs) in 0-4 yr old children, through mortality risk only, by region.

Region	DALYs lost		Goiter	Population Attributable Risk	DALYs lost from IDDs	DALYs remaining after eliminating IDDs	% reduction	
	from all causes	from Group 1 diseases	prevalence %				Grp I	all causes
India	108,106,668	90,221,012	10	0.091	8,201,910	82,019,102	9.1	7.59
China	35,277,161	23,435,979	10	0.091	2,130,544	21,305,435	9.1	6.04
Other Asia	53,629,202	46,407,277	20	0.167	7,734,546	38,672,731	16.7	14.42
SS Africa	133,369,079	122,124,409	15	0.130	15,929,271	106,195,138	13.0	11.94
LAmCa	23,316,124	18,976,535	10	0.091	1,725,140	17,251,395	9.1	7.40
MEC	60,705,419	51,274,604	20	0.167	8,545,767	42,728,837	16.7	14.08
Total	414,403,653	352,439,816			44,267,178	308,172,638	12.6	10.68

Table 10

Summary of direct and indirect contributions of malnutrition to the burden of disease in developing countries, by group (with % of total burden, all groups all causes, in brackets).

Cause	Group	DALYs lost (% overall total burden)				As % of group DALY loss
		Direct (from deficiency itself)		Indirect (as risk factor)	Total (with new estimate)	
		Previous estimate	New estimate			
General malnutrition/ underweight	0-4 yrs (mortality + morbidity)	11,465,000 [1] (1.0%)	11,465,000 (1.0%)	169,490,893 [2] (14.0%)	180,955,893 (15.0%)	35.0% [3]
Vitamin A deficiency	0-4 yrs (mortality only)	11,757,000 [4] (1.0%)	11,757,000 (1.0%)	54,753,335 [5] (4.5%)	66,510,335 (5.5%)	16.0% [6]
Iron deficiency	Reproductive aged women (15-49 y) (direct, mortality + morbidity; indirect, mortality only)	3,901,000 [7] (0.3%)	39,754,176 [8] (3.3%)	3,601,000 [9] (0.3%)	43,355,176 (3.6%)	27.6% [10]
Iodine deficiency disorders	All ages (direct, mortality + morbidity) 0-4 yrs (indirect, mortality only)	5,711,000 [11] (0.5%)	57,384,000 [12] (4.7%)	-- 44,267,178 [13] (3.7%)	101,651,600 (8.4%)	8.4% [14]
Total		32,834,000 (2.7%)	120,360,176 (10.0%)	272,112,406 (22.5%)	392,473,004 (32.4%)	32.4%[15]

Notes:

1 From Murray and Lopez (1994), Annex tables 6-11, group II.D1 -- protein-energy malnutrition -- summed for developing countries: 0-4 years, both sexes, mortality plus morbidity.

2 From Table 5 here.

3 Denominator = 516,407,014 DALYs, from Murray and Lopez (1994) Annex tables 6-11, summed for developing countries, all causes, 0-4 years, mortality plus morbidity.

4 From Murray and Lopez (1994), Annex table 6, group II.D3; summed for developing countries: 0-4 years, both sexes.

5 From Table 7 here.

6 Denominator = 414,403,653 DALYs, from Murray and Lopez (1994) Annex table 6, summed for developing countries, all causes, 0-4 years, mortality only; (direct DALY losses were assigned to morbidity by Murray and Lopez, however assigning to mortality is more plausible, given low prevalences (about 1%) of clinical deficiency, and its high risk; thus the denominator is mortality DALYs).

7 From Murray and Lopez (1994), Annex tables 6-11, group II.D4 -- anaemias -- summed for developing countries, women 15-44 years: mortality plus morbidity.

8 Calculated as (population of 15-44 yr women) * (prevalence of anemia) * (0.096). Prevalence is from Mason et al (2001), table 4, p29, (applied ignoring the higher prevalence among pregnant women). The disability factor of 0.096 is the class1 weighting from Murray and Lopez (1994), table 2, p12.

9 From table 8 here: refers to estimated reduction in maternal mortality from preventing severe anemia.

10 Denominator = 157,080,000 DALYs, from Murray and Lopez (1994) Annex tables 6-11,summed for developing countries, all causes, women 15-44 years: mortality plus morbidity.

11 From Murray and Lopez (1994), Annex tables 6-11, group II.D2 -- iodine deficiency -- summed for developing countries, all ages, both sexes: mortality plus morbidity.

12 Calculated as (population, all ages, both sexes) * (prevalence of goiter) * (0.096). Prevalence is from Mason et al (2001), table 8, p34. The disability factor of 0.096 is the class1 weighting from Murray and Lopez (1994), table 2, p12.

13 From table 9 here.

14,15 Denominator = 1,210,106,000 DALYs, i.e. total developing country DALYs, all groups, all causes, mortality plus morbidity: from Murray and Lopez (1994) Annex tables 6-11 summed for developing countries.

Table 11

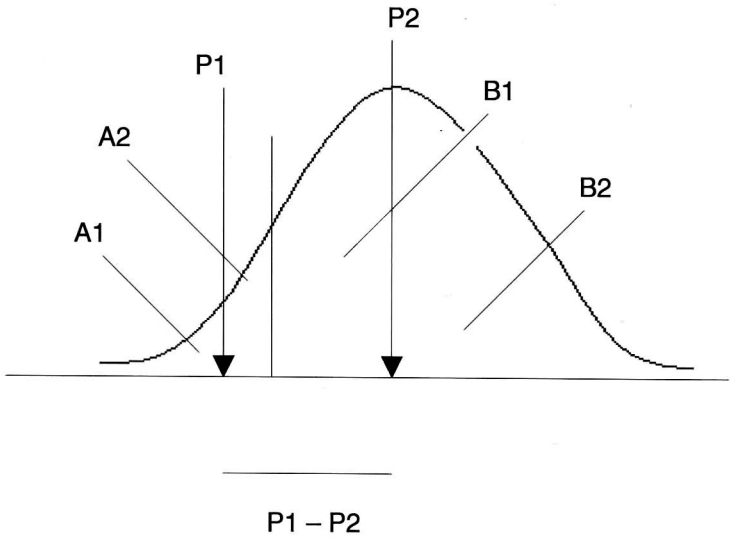
Contributions (%) of malnutrition to the burden of disease, by region and deficiency.

Region	% total DALY loss for group; total DALYs; as % all cause, all groups, all developing countries					
	Underweight (0-4 y)	Vitamin A deficiency (0-4 y)	Iron deficiency in women 15-44 yrs		Iodine deficiency disorders (all ages)	Total
			anemia	maternal mortality		
India	46.6% 63,611,655 5.26	23.1% 24,929,234 2.06	28.2% 10,030,176 0.83	14.4% 1,123,000 0.09	6.4% 18,803,670 1.55	40.3% 118,497,735 9.79
China	22.3% 11,076,180 0.92	6.6% 2,315,565 0.19	29.1% 9,218,477 0.76	9.1% 226,000 0.02	5.9% 11,925,712 0.99	17.3% 34,761,934 2.87
Other Asia	32.9% 22,003,835 1.82	16.9% 9,061,743 0.75	38.5% 8,733,312 0.72	14.1% 614,000 0.05	9.2% 16,252,146 1.34	32.1% 56,665,036 4.68
Sub-Saharan Africa	40.4% 63,297,041 5.23	17.2% 22,980,185 1.90	10.4% 3,731,443 0.31	13.2% 1,054,000 0.09	8.1% 23,571,524 1.95	39.2% 114,634,193 9.47
Latin America & Caribbean	16.8% 5,433,632 0.45	11.1% 2,579,107 0.21	19.1% 2,998,080 0.42	9.2% 166,000 0.01	11.2% 11,492,631 0.95	22.0% 22,669,450 1.87
M. Eastern Crescent	20.9% 15,533,550 1.28	7.7% 4,644,501 0.38	32.5% 5,042,688 0.25	9.9% 418,000 0.03	13.6% 19,605,917 1.62	31.4% 45,244,656 3.74
Total	35.0% 180,955,893 14.95	16.0% 66,510,335 5.50	25.3% [1] 39,754,176 3.28	12.6% [1] 3,601,000 0.30	8.4% 101,651,600 8.40	32.4% 392,473,004 32.43

[1]These average 27.6%, as shown in table 10.

Figure 1

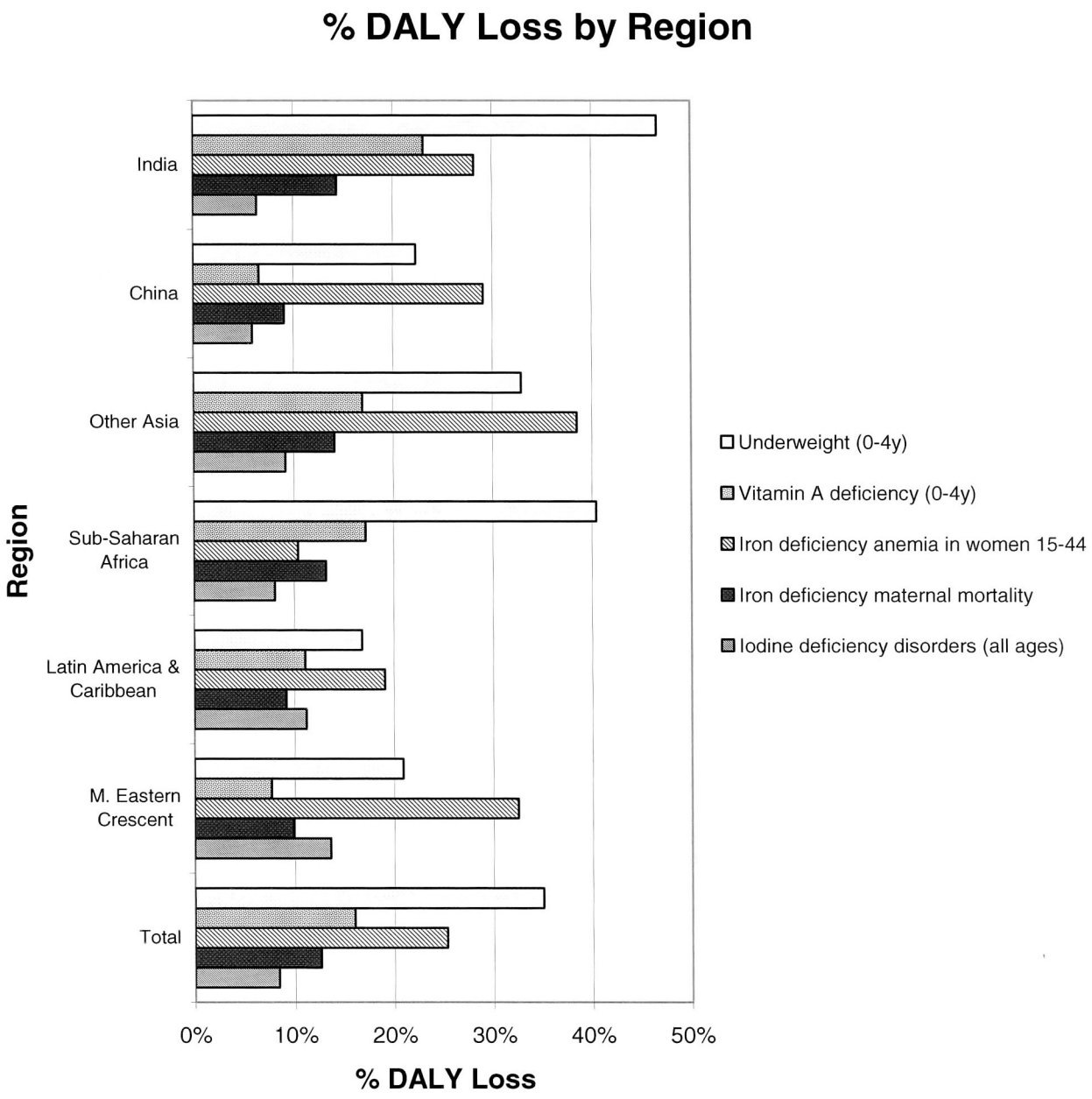
Illustration of calculation of interval distance between two groups above and below cut-off (e.g. > & < -2SDs)



Symbols: P1 is where area A1 = A2; P2 is where B1 = B2; distance between groups is P1 – P2

Figure 2

Contributions of malnutrition to the burden of disease, as % of burden that would be removed by eliminating different forms of malnutrition in the groups indicated.



Annex: Sources

Literature extracted to investigate relations of child anthropometry with mortality and morbidity.

	Country	Source
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1. At Least One-Third Of Poor Countries' Disease Burden Is Due To Malnutrition. By John B. Mason, Philip Musgrove and Jean-Pierre Habicht. March 2003.

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